

**Amendments to the Drawings:**

Please replace FIGS. 1-17 with the attached replacement sheets of drawings for FIGS. 1-17.

**REMARKS/ARGUMENTS**

**I. Status of the Claims**

Claims 1-8 and 10-29 are pending. Claim 9 is cancelled. Claims 16-23 have been withdrawn. Claims 28 and 29 are new. Claims 1-8, 10-15 and 24-29 are under consideration. Claims 1, 2, 4-6, 8, 10, 15 and 24-25 are amended.

**II. Support for Amendments to the Claims**

Applicants have amended claims 1, 2, 4-6 and 25 to add the term "macrocyclic". This amendment has been made to provide a proper antecedent basis for the terms metal chelate or chelate discussed in these claims. Because this amendment is correcting a minor error in form, support is not required.

Claim 3 is amended to add the term OR<sup>1</sup> to Z<sup>1</sup> and Z<sup>2</sup>. Support for this amendment is found in originally filed claim 5.

Claim 6 is amended to add a description of the terms R<sup>1a</sup> and R<sup>4a</sup>. Support for this amendment is found in originally filed claim 3.

Claim 8 is amended in order to change the claim dependency from 5 to 6. This amendment has been made to provide a proper antecedent basis for the carbon atom marked \* discussed in these claims. Because this amendment is correcting a minor error in form, support is not required.

Claim 10 is amended to clarify that the antibody is specifically binding to the cell surface antigen which is described in claim 1. Because this amendment is correcting minor errors in form, support is not required.

Claim 15 is amended in order to change the claim dependency from 1 to 14. This amendment has been made to provide a proper antecedent basis for the term mammal discussed in these claims. Because this amendment is correcting a minor error in form, support is not required.

**III. IDS Objection**

On page 3 of the Detailed Action of the Office Action mailed June 22, 2005, the Examiner states that reference WO 00/74729 A2 was submitted with the IDS submitted on October 29, 2003 but not cited therewith. In a telephone conference with Examiner Fetterolf on July 5, 2005, Kathryn Degliantoni explained that the reference was cited and Examiner Fetterolf agreed that the reference was overlooked. Applicants respectfully request that reference WO 00/74729 be considered and that Examiner Fetterolf initial a copy of the PTO-1449 form listing said reference.

**IV. Specification Objection and amendments to the Drawings**

The Figures in the specification are objected to for improper disclosure of amino acid sequences and nucleotide sequences without a respective sequence identifier. Applicants have added sequence identifiers to the Figures and the written description, which are included in this Response. Since the sequences in the specification are now properly identified, Applicants respectfully request withdrawal of this objection.

Thirty-two (32) replacement sheets of drawings, containing FIGS. 1-17, are submitted herein. In particular, amendments to FIGS. 1-11 have been made to provide sequence identifiers per 37 CFR 1.821 through 1.825. Additionally, sequences of FIGS. 3A, 5, 6, 7A, 7B, 8, 9A, and 9B, which previously spilled over onto several sheets, have been reorganized in the replacement sheets of drawings provided. As such, withdrawal of the objection is respectfully requested.

**V. Claim Objection**

Claim 8 is objected to for lacking an antecedent basis for the carbon marked “\*”. Applicants have amended claim 8 to depend from claim 6. Applicants respectfully request that this amendment be entered in the record.

**VI. Claim Rejections Under 35 U.S.C. § 102**

To maintain a *prima facie* case of anticipation, the Examiner must demonstrate that each and every element as set forth in the claim is either expressly found or is inherently

described in a single prior art reference. The identical invention must be shown in as complete detail as is contained in the ...claim. See MPEP § 2131. Applicants submit that each element of the claims now pending has not been identified in the art presently of record. Therefore, Applicants respectfully traverse the following rejections.

Under § 102(a) over Sharkey

Claims 1-8, 10-14 and 24-27 are rejected under 35 U.S.C. § 102(a) as allegedly being anticipated by Sharkey, *et al.* (2002 ASCO Annual Meeting Abstract, Orlando, Fl., May 18, 2002) (“Sharkey”). Sharkey is cited by the Examiner for teaching a method of treating cancer in a subject by, among other things, administering an antibody that recognizes a targetable conjugate. In Sharkey’s case, the targetable conjugate is a DOTA chelate with a tripeptide side chain (histamine-succinyl-glycyl). While Sharkey’s antibody recognizes a targetable conjugate, the antibody is only recognizing a peptide sequence on the conjugate, and not the macrocyclic metal chelate itself. Therefore, any chelate, or any other molecule, could replace the macrocyclic metal chelate on Sharkey’s targetable conjugate and binding would be the same, so long as the tripeptide side chain is not manipulated or interfered with. Therefore, Sharkey is missing Applicant’s element of “antigen recognition domain that recognizes a macrocyclic metal chelate”. Since all the elements of the Applicant’s invention are not present in Sharkey, the anticipation rejection cannot be maintained.

Under § 102(b) over Hansen

Claims 1-8, 10-15 and 24-27 are rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Hansen, *et al.* (US 2002/0006379, 1/17/2002) (“Hansen”). Hansen is cited by the Examiner for teaching a method of treating cancer in a subject by, among other things, administering an antibody that recognizes a targetable conjugate. In Hansen’s case, the targetable conjugate is a DOTA chelate with a peptide side chain. While Hansen’s antibody recognizes a targetable conjugate, the antibody is only recognizing a peptide sequence on the conjugate, and not the macrocyclic metal chelate itself. Therefore, any chelate, or any other molecule, could replace the macrocyclic metal chelate on Hansen’s targetable conjugate and binding would be the same, so long as the peptide side chain is not manipulated or interfered

with. Therefore, Hansen is missing Applicant's element of "antigen recognition domain that recognizes a macrocyclic metal chelate". Since all the elements of the Applicant's invention are not present in Hansen, the anticipation rejection cannot be maintained.

Applicants respectfully request the withdrawal of these rejections.

**VII. Claim Rejections Under 35 U.S.C. § 112, second paragraph:**

Applicants respectfully traverse the following rejection.

*Over Claim 4*

Claim 4 is rejected under 35 U.S.C. 112, second paragraph as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Support for this claim is found in the specification on page 56, lines 15-23. Therefore, Applicants respectfully request withdrawal of this rejection.

**VIII. Claim Rejections Under 35 U.S.C. § 112, first paragraph, written description:**

Claims 1-4 and 10-15 are rejected under 35 U.S.C. 112, first paragraph as allegedly failing to comply with the written description requirement. Applicants respectfully traverse.

The written description requirement is satisfied when a representative number of species of the claimed invention are described. This principle is exemplified by *In re Herschler*, 200 USPQ 711 (C.C.P.A. 1979) ("*Herschler*"); MPEP § 2163(II)(A)(3)(a)(ii). In that case, the claimed invention was the use of DMSO to enhance delivery of physiologically active steroids, and the specification provided one example demonstrating the efficacy of the claimed methods. The Patent Office rejected the claims, in part, for lack of written description for not disclosing a representative number of physiologically active steroids. The C.C.P.A. reversed the Patent Office's rejection of these claims, reasoning that, because the invention was not the discovery of novel steroidal agents but a method of delivering the agents in combination with DMSO, explicit written disclosure of all steroidal agents was not required to meet the written description requirement. Therefore, the written description requirement does not require all species of every claim term to be disclosed; rather, only an adequate description of the claimed invention.

In the present case, the claimed invention is not a mutant antibody. Rather, the invention is a novel method of using these mutant antibodies to treat cancer. As shown in *Herschler*, one example can adequately describe the claimed methods for written description purposes. Applicants have described the use of antibodies, such as 2D12.5, in methods of treating cancer on pages 60-63 of the specification. Due to this disclosure, Applicants have complied with the written description requirements as described by the MPEP and *Herschler*. Therefore, a written description rejection cannot be maintained. Accordingly, withdrawal of the rejection is respectfully requested.

**IX. Claim Rejections Under 35 U.S.C. § 112, first paragraph, enablement:**

Claims 1-27 are rejected under 35 U.S.C. § 112, first paragraph, because the specification and prior art, while being enabling for a method of treating cancer in a subject comprising administering an antibody comprising an antigen recognition domain that recognizes a macrocyclic metal chelate such as DOTA, wherein said antibody comprises a targeting moiety, anti-CEA, that binds to a cancer cell by binding with a cell surface antigen; and administering to said subject a metal chelate, allegedly does not reasonably provide enablement for a method of treating any cancer in a subject comprising administering any and/ or all antibodies comprising an antigen recognition domain that recognizes a macrocyclic metal chelate, wherein said antibody comprises any and /or all targeting moieties which bind to a cancer cell by binding to any and / or all cell surface receptors and cell surface antigens; and a macrocyclic metal chelate. Applicants traverse.

Applicants have provided adequate teachings on how to make and use the antibodies of the invention for treating cancer. These methods are described on pages 60-63 of the specification. Due to this disclosure, Applicants have complied with the enablement requirement as described by the MPEP. Therefore, an enablement rejection cannot be maintained. Accordingly, withdrawal of the rejection is respectfully requested.

**X. Response to Provisional Obviousness-type Double Patenting Rejections**

*Over Co-pending Application No. 10/350,555*

Claims 1-8 and 10-15 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting over claims 34-36 and 35-37 of U.S. Pat. App. No. 10/350,555 (Meares). The Examiner states that a timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome this rejection. Applicants would be happy to consider the filing of a terminal disclaimer in this case once claims have been found allowable in U.S. Pat. App. No. 10/350,555. Until that time, Applicants respectfully request that the double patenting rejection be held in abeyance.

*Over Co-pending Application No. 10/631,258*

Claims 1-8 and 10-15 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting over claims 34-36 and 35-37 of U.S. Pat. App. No. 10/631,258 (Meares). The Examiner states that a timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome this rejection. Applicants would be happy to consider the filing of a terminal disclaimer in this case once claims have been found allowable in U.S. Pat. App. No. 10/631,258. Until that time, Applicants respectfully request that the double patenting rejection be held in abeyance.

**XI. Change of Correspondence Address and Attorney Docket No.**

Please address all future correspondence in this case to:

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Also, please change the Attorney Docket No. to 61818-5015-US01.

Appl. No. 10/625,047  
Amdt. dated December 22, 2005  
Response to Office Action dated June 22, 2005

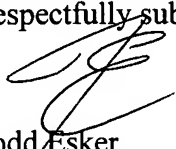
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**CONCLUSION**

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-442-1000.

Respectfully submitted,



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Attachments

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